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10/519,826	09/14/2005	Diego Walther	BB-123	3100

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EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
ART UNIT	**PAPER NUMBER**
1652	

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02/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,826	WALTHER ET AL.	
	Examiner	Art Unit	
	IQBAL H. CHOWDHURY	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21,24-26 and 28* is/are pending in the application.

4a) Of the above claim(s) *1,4-21,24 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-3 and 25-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

Claims 1-21, 24-26 and 28 are currently pending in the instant Office action.

In response to a previous Office action, a non-final action (mailed on July 5, 2007), Applicants filed a response and amendment received on December 5, 2007, amending claims 2 and 25, and canceling claim 27 is acknowledged. Claims 1, 4-21, 24 and 28 remain withdrawn as drawn to nonelected invention. Claims 22 and 23 remain cancelled.

Claims 2-3 and 25-26 are under consideration and will be examined herein.

Applicants' arguments filed on December 5, 2007, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

New - Claim Objection

Claims 2 and 26 are objected to in the recitation of "tryptophane hydroxylase", which should be "tryptophan hydroxylase". Appropriate correction is required.

Claim 2 is objected to in the recitation of "sn-TPH", as abbreviations should not be used without at least once fully setting forth what they are used for. Appropriate correction is required.

Maintained - Claim Rejections - 35 U.S.C. § 112

Previous rejection of claims 25 and 26 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. This rejection has been

discussed at length in the previous Office action. The rejection is maintained for the following reasons.

Claims 25 and 26 are directed to a combination therapeutic comprising any polypeptide of SEQ ID NO: 2 encoded by the nucleic acid sequence of SEQ ID NO: 1 having degenerated genetic code or any derivatives of a polypeptide encoded by SEQ ID NO: 1 or any polypeptide having 90% identity to a polypeptide encoded by SEQ ID NO: 1 or any polypeptide having sn-TPH activity exhibit polymorphisms and an additional protein involve in serotonin metabolism (claim 25) or an additional protein any peripheral tryptophan hydroxylase (claim 26), which is characterized in increased or decreased peripheral and neuronal serotonin production.

Applicants argue (pages 9 and 10 of the Remarks) that "the examiner focuses on the recitation, in claim 25, of at least one additional protein or the regulation of the serotonin metabolism and, in claim 26, of the additional protein being a peripheral tryptophan hydroxylase. Applicants also argue that in the current case the point of novelty of the invention is the new use for the claimed protein and having identified this new use, the inventors also envisioned the use of this protein with other proteins for regulating serotonin metabolism. Applicants further argue that these other proteins are not being claimed; rather it is merely their use in combination with the protein of the subject invention that is being claimed. Such other proteins would be known to, and readily envisioned by, those skilled in the art having the benefit of the current disclosure. An analogous situation would be a claim to the use of a new chemotherapy agent in combination with an analgesic. Surely, an applicant making such a claim would not be required to disclose multiple examples of analgesics in order to meet the written description requirement. Recent court decisions have made it clear that compliance with the written description requirement does

not require the type of disclosure that has been set forth as necessary in the outstanding Office Action. See, for example, Capon v. Eshhar, 418 F.3d 1349, 1357, 76 USPQ2d 1078, 1084 (Fed. Cir. 2005)".

Applicant's arguments have been fully considered but are not deemed to be persuasive to overcome the rejection on written description issues. Claims 25 and 26 are directed to a combination therapeutic comprising the polypeptide of SEQ ID NO: 2 and an additional protein, which is involve in serotonin metabolism, wherein said additional protein is any peripheral tryptophan hydroxylase, including mutants and variants. In particular, claim 25 still reads on any additional protein for the regulation of serotonin metabolism, which is enormously broad and one of ordinary skill in the cannot practice the claimed invention without knowing the structure and functional relationship of the additional protein used to make combination therapeutic. The second constituents of the combination therapeutic is a very important protein, which is similar in function of the first constituents, and the combination of the two must have a specific aim and objective, which needs the fulfillment of the written description requirement, i.e. structural and functional correlation. The second polypeptide of the therapeutics is not like pharmaceutical acceptable excipient or carrier, but an important specific protein. Claim 26 also still reads on using any peripheral tryptophan hydroxylase having no structure. Claims are thus drawn to a combination therapeutic comprising the polypeptide of SEQ ID NO: 2 and an additional protein, wherein said additional protein is any peripheral tryptophan hydroxylase, wherein said protein structure is not fully described in the specification. No information, beyond the characterization of a protein having tryptophan hydroxylase activity in the peripheral region. The specification does not contain any disclosure of the structure of all the mutants or variants of any peripheral

tryptophan hydroxylase used to make combination therapeutic in the claim, that is required for fulfilling Written description requirements. As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient structure and variety of species to reflect the representative structure variation within the genus.** Satisfactory disclosure of a representative structure and number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of species disclosed. For inventions in an unpredictable art, adequate written description of a genus, cannot be achieved by disclosing the structure of small portion of only one species within the genus. The genus of polypeptide having peripheral tryptophan hydroxylase activity is structurally diverse as it broadly encompasses many mutants, and variants having different structures. As such, the disclosure solely of functional features that may or may not present in all members of the genus is insufficient to be representative of the attributes and features of the entire genus. Therefore, the rejection is maintained.

Maintained - Claim Rejections - 35 U.S.C. § 112

Previous rejection of Claims 2 and 25-26 under U.S.C. 112, first paragraph, enablement requirement, is maintained. This rejection has been discussed at length in previous Office Action. The rejection is maintained for the following reasons.

The specification, while being enabling for the polypeptide of SEQ ID NO: 2 from human or a combination therapeutic of the protein of SEQ ID NO: 2 with peripheral tryptophan hydroxylase of GenBank Accession No. P17752 from human, does not reasonably provide enablement for any tryptophan hydroxylase which is 90% identical to SEQ ID NO: 2 and a combination with thereof with any additional protein involve in serotonin metabolism (claim 25) from any source or an additional protein of any peripheral tryptophan hydroxylase (claim 26) from any source, which is characterized in increased or decreased peripheral and neuronal serotonin production. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed invention commensurate in scope with these claims.

Applicants argue (in page 10 of the Remarks) that "a person skilled in the art could readily, and without undue experimentation practice the full scope of the invention as now claimed and further states that the applicants have amended claim 2 herein to recite 90% homology to the exemplified sequence. Support for this amendment can be found at, for example, page 7, first full paragraph of the specification as filed, and given the high level of skill in this art, as well as the guidance provided in the applicants' specification, a person skilled in the art could readily practice the subject invention with closely-related sequences as now claimed".

Applicants' arguments have been fully considered but are not deemed to be persuasive to overcome the rejection on scope of enablement issues.

Claims 2, 25 and 26 are so broad as to encompass any polypeptide which is 90% identical to SEQ ID NO: 2 and a combination therapeutic thereof with any additional protein involve in serotonin metabolism (claim 25) from any source or an additional protein of any peripheral tryptophan hydroxylase (claim 26) from any source. The amended claim 2 still recites a polypeptide, which is 90% identical to SEQ ID NO: 2 and a combination therapeutic thereof, i.e. 10% non-identical that means 49 amino acids are different at any position of said 490 amino acids protein, which includes many mutants and variants. Claims 25 and 26 still recite using any protein having any structure involved in serotonin metabolism (claim 25) or any peripheral tryptophan hydroxylase having any structure, which includes many mutants and variants that would be used in addition of the protein of claim 2 in making the composition.

Guo et al. (Protein tolerance to random amino acid change, Proc Natl Acad Sci U S A, 2004 Jun 22; 101(25): 9205-10, Epub 2004 Jun 14) teach that the percentage of random single substitution mutations which inactivate a protein for the protein 3-methyladenine DNA glycosylase is 34% and that this number appears to be consistent with other studies in other proteins as well. Guo et al. further show in Table 1 that the percentage of active mutants for multiple mutants appears to be exponentially related to this by the simple formula $(.66)^x$ X 100% where x is the number of mutations introduced. Applying this estimate to the instant protein 90% identity allows up to 49 mutations within the 490 amino acids of SEQ ID NO: 2 and thus only $(.66)^{49}$ X 100% or 1.4 x 10^{-7}% (i.e. $\cong$ 1 in 14 million) of random mutants having 90% identity would be active. Current techniques (i.e., high throughput mutagenesis and screening

techniques) in the art would allow for finding a few active mutants within several hundred thousand or up to about a million inactive mutants as is the case for the claims limited to 95% identity (despite even this being an enormous quantity of experimentation that would take a very long time to accomplish) but finding a few mutants within many millions or more as in the claims to 90% or less identity would not be possible. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification.

While methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan, producing variants useful as tryptophan hydroxylase to use in neuronal disease requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the activity. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. For the rejected claims, this would clearly constitute **undue** experimentation.

Sufficient guidance has **not** been provided in the instant specification or in the prior art as at best art teaches to avoid changes of 10% of the structure of SEQ ID NO: 2 but does little to suggest what changes would be successful particularly for those enzymes having the substantial number of alterations necessary to produce a protein having 90% identity to SEQ ID NO: 2.

For all the reasons as discussed above and in the previous Office action, the rejection is maintained.

Maintained-Claim Rejections - 35 USC § 102

Previous rejection of Claims 2-3 under 35 U.S.C. 102(b) as being anticipated by Yu et al. (WO/2002/97039, publication 12/5/2002, claim priority of US application 60/294076, filed on 5/29/2001, see IDS) is maintained. Instant claims drawn to an isolated polypeptide of SEQ ID NO: 2 having tryptophan hydroxylase activity.

Yu et al. teach a polypeptide having 100% identity to SEQ ID NO: 2 of the instant application as well as the nucleotide sequence, encoding thereof. Yu et al. also teach that said polypeptide is a tryptophan hydroxylase isolated from human, which is highly similar in terms of structure to animal hydroxylase (p 1-3 and 21-22). Yu et al. further teach variants of said human tryptophan hydroxylase. Furthermore, Yu et al. teach that said polypeptide could be used as pharmaceutical composition for therapeutic treatment related to anxiety, depression, hyperactivity or sleep disorder. Therefore, Yu et al. anticipate claim 2-3 of the instant application.

Applicants argue (in pages 10-12 of the Remarks) that "Yu *et al.* reference does not disclose each and every element of the applicants' claimed invention and further argue that it is a basic premise of the Patent Law that, to anticipate, a single reference must, within its four corners, disclose all of the limitations of the claimed invention. Applicants also argue that WO 2002/97039 merely discloses that the proteins of WO 2002/97039 share structural similarity with animal hydroxylases, and particularly tryptophan hydroxylases, which are involved in a rate-limiting step in the biosynthesis of a number of neurologically active compounds, including, but not limited to, DOPA, serotonin and melatonin" (page 2, lines 1 - 5). Applicants further argue that WO 2002/97039 does not disclose any biological data verifying the function of the proteins

of WO 2002/97039, and thus, neither the nucleic acid sequence depicted in SEQ ID No. 1 nor the polypeptide according to SEQ ID No. 2 of WO 2002/97039 are biologically validated. More importantly, in addition, it is nowhere stated that the polypeptide depicted in SEQ ID No. 2 functions as a neuronal tryptophan hydroxylase (snTPH)".

This is not found persuasive because Yu et al. indeed teach a tryptophan hydroxylase protein from human, which is 100% identical to SEQ ID NO: 2 of the instant application, inherently a neuronal tryptophan hydroxylase (see sequence alignment). The function and identifying characteristics of a protein are the inherent properties of said protein.

Furthermore, applicants argue that "for a claim to be anticipated under the principles of inherency, the subject of a single prior art reference must necessarily function in accordance with the limitations of the process or method claimed. Further, the doctrine of inherency is available only when the prior inherent event can be established as a certainty. A prior inherent event cannot be established based on speculation, or where a doubt exists (emphasis added). The cited reference does not disclose with any certainty that the proteins disclosed therein would, in fact, have the activity claimed by the current applicant".

This is not found persuasive because inherency is also applicable to product claim. There is no speculation but the direct evidence that claimed protein is 100% identical to the protein of Yu et al. and indeed a tryptophan hydroxylase and inherently comprises tryptophan hydroxylation function and inherently a neuronal tryptophan hydroxylase including sn-THP.

Because the protein of the instant application and that of the reference is one and the same, Examiner takes the position that the structure of the disclosed in the reference inherently has the same function as in the claimed protein. Since the Office does not have the facilities for

examining and comparing applicants' protein function with the protein function of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein).

Therefore, the rejection is maintained.

Maintained-Claim Rejections - 35 USC § 103

Previous rejection of Claims 25-26 under 35 U.S.C. 103 (a) as being obvious over Yu et al. (WO/2002/97039, publication 12/5/2002, claim priority of US application 60/294076, filed on 5/29/2001, see IDS) as applied to claim 2-3 above in view of Wang et al. (J Neurochem. 1998 Oct; 71(4): 1769-72) and Veenestra-VanderWeele et al. (Knockout mouse points to second form of tryptophan hydroxylase, Mol Interv. 2003 Mar; 3(2): 72-5, 50. Review). Instant claims drawn to a therapeutic composition comprising an isolated polypeptide of SEQ ID NO: 2 having tryptophan hydroxylase activity and an additional polypeptide having serotonin metabolic activity.

Yu et al. teach a polypeptide having 100% identity to SEQ ID NO: 2 of the instant application as well as nucleotide sequence. Yu et al. also teach that said polypeptide is human tryptophan hydroxylase having tryptophan hydroxylase activity. Yu et al. further teach variants of said tryptophan hydroxylase having tryptophan hydroxylase activity. Furthermore, Yu et al. teach that said polypeptide could be used as pharmaceutical composition for therapeutic treatment related to anxiety, depression, hyperactivity or sleep disorder (see pages 1-5, 21 and

22). Yu et al. do not teach a composition comprising said tryptophan hydroxylase protein and an additional peripheral tryptophan hydroxylase protein having serotonin metabolism activity.

Wang et al. teach two alternative splicing at the 3'-cDNA of human tryptophan hydroxylase, which give rise to two isoforms of human tryptophan hydroxylase i.e. one is short form TPH1 i.e. spliced (444 amino acids) and another is long form TPH2 i.e. un-spliced (490 amino acids), which is neuronal specific. Wang et al. do not clearly teach functional significance of these two isoforms.

However, Veenestra-VanderWeele et al. teach two isoform of TPH, specifically also neuronal specific TPH2 expression in brain. Veenestra-VanderWeele also teach by knockout inactivation of TPH1 (which is peripheral TPH) results in no serotonin production in the gut with no behavioral change but significant serotonin production in brain due to the presence of TPH2, which indicates that TPH2 (neuronal) is more potent than TPH1 in terms of serotonin metabolism.

Since, Yu et al. clearly teach said tryptophan hydroxylase, a serotonin metabolic enzyme and a composition comprising said protein for using as therapeutic, it would have been obvious to one to ordinary skill in the art at the time of the invention was made to make a therapeutic composition comprising said neuronal tryptophan hydroxylase protein and an additional splice variant of tryptophan hydroxylase of Wang et al. and Veneestra-VanderWheele et al. for increased serotonin production for a making a pharmaceutical composition for treating diseases like anxiety, depression, or sleep disorder.

One of ordinary skill in the art would have a reasonable expectation of success in making a therapeutic composition comprising the polypeptide of Yu et al. and adding another splice

variant of tryptophan hydroxylase protein of Wang et al. to enhance the serotonin production for treating disease related to anxiety, depression, hyperactivity or sleep disorder.

One of ordinary skill in the art would have a reasonable expectation of success because Yu et al. suggested to make a composition comprising said protein could be used for therapeutic purpose.

Applicants argue (in pages 12-13 of the Remarks) that "the shortcomings of the primary Yu *et al.* reference with respect to the current invention have been discussed above in detail and the secondary references cited in support of this obviousness rejection do not cure or even address the aforementioned deficiencies of the primary reference. Applicants also argue that the protein depicted in SEQ ID No.2 of the present invention has been identified as a specifically neuronal isoform of tryptophan hydroxylase, in contrast, the protein according to SEQ ID No.2 of WO 2002/97039 is only *assumed* to have a general tryptophan hydroxylase activity, wherein there is no distinction between peripheral and neuronal tryptophan hydroxylase activity. Thus, WO 2002/97039 fails to disclose that the protein depicted in SEQ ID No.2 of WO 2002/97039 is a specifically neuronal isoform of tryptophan hydroxylase. Applicants further argue that without this knowledge there would be no reason to propose the combination therapeutic composition as set forth in claim 25. It has been well established in the patent law that the mere fact that the purported prior art could have been modified or applied in some manner to yield an applicant's invention does not make the modification or application obvious unless "there was an apparent reason to combine the known elements in the fashion claimed" by the applicant. Furthermore, an applicant's invention is not "proved obvious merely by demonstrating that each of its elements was, independently, known in the (purported) prior art." An assertion of obviousness without the

required suggestion or expectation of success in the prior art is tantamount to using the applicant's disclosure to reconstruct the prior art to arrive at the subject invention. The cited references, either alone or in combination, do not provide a suggestion of the claimed invention and, certainly, no expectation of success".

This is not found persuasive because Yu et al. indeed teach a tryptophan hydroxylase protein from human, which is 100% identical to SEQ ID NO: 2 of the instant application, inherently a neuronal tryptophan hydroxylase (see sequence alignment), and a composition comprising said protein. The function and identifying characteristics of a protein are the inherent properties of a protein. Yu et al. indeed mentioned that said protein is human tryptophan hydroxylase protein, which is also similar to animal tryptophan hydroxylase protein. There is no shortcoming or deficiency of Yu et al. reference as discussed above because the product (protein) of the reference and the product (protein) of the instant application is the same. In addition, inherency is applicable to product claim as well as process claim. Besides, the primary reference Yu et al. meet the part of claim 25 limitation and rest of them is taught by secondary references Wang et al. and Veenestra-VanderWeele et al.

As discussed previously, Since, Yu et al. clearly teach said tryptophan hydroxylase (which is 100% identical to SEQ ID NO: 2 of the instant application), a serotonin metabolic enzyme and a composition comprising said protein for using as therapeutic, it would have been obvious to one to ordinary skill in the art at the time of the invention was made to make a therapeutic composition comprising said neuronal tryptophan hydroxylase protein and an additional splice variant of tryptophan hydroxylase of Wang et al. and Veneestra-VanderWheele

et al. for increased serotonin production for a making a pharmaceutical composition for treating diseases like anxiety, depression, or sleep disorder.

One of ordinary skill in the art would have a reasonable expectation of success in making a therapeutic composition comprising the polypeptide of Yu et al. and adding another splice variant of tryptophan hydroxylase protein of Wang et al. to enhance the serotonin production for treating disease related to anxiety, depression, hyperactivity or sleep disorder.

One of ordinary skill in the art would have a reasonable expectation of success because Yu et al. suggested to make a composition comprising said protein could be used for therapeutic purpose.

Besides, **Supreme Court** decision on *KSR Int'l v. Teleflex, Inc.* further strengthen the TSM test (teaching, suggestion and motivation) to combine the prior art elements to meet the claimed subject matter (see KSR Int'l Co. V. Teleflex, Inc., No 04-1350, US Apr. 30, 2007). Therefore, the rejection is maintained as discussed.

Conclusion

Claims 1-21, 24-26, 28 are pending.

Claims 1, 4-21, 24 and 28 are withdrawn.

Claims 2-3 and 25-26 are rejected.

THIS ACTION IS MADE FINAL. See M.P.E.P. 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury, Ph.D. whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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